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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/825,219	04/16/2004	Alfons Bosman	BJS-2551-149	7081

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EXAMINER	
BOESEN, AGNIESZKA	
ART UNIT	PAPER NUMBER
1648	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/22/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/825,219	BOSMAN ET AL.	
	Examiner	Art Unit	
	Agnieszka Boesen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12-23* is/are pending in the application.

4a) Of the above claim(s) *21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12-20,22 and 23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 April 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *November 14, 2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Amendment filed November 14, 2006 in response to the Office Action of August 14, 2006 is acknowledged and has been entered. Claims 12-20, 22, and 23 are currently being examined. No claims have been amended.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Information Disclosure Statement

The Information Disclosure Statements received November 11, 2006 has been considered and the copies are attached to this Office Action.

Drawings

Applicant requested a confirmation that the figures filed April 16, 2004 are acceptable. The drawings filed April 16, 2004 are in compliance with 37 CFR 1.121). Thus the figures are acceptable.

Foreign Priority

The certified copy of the foreign priority document EP 99870225.2 has been received. The foreign priority document EP 94870132 received by the Patent Office in the parent application 08/612,973 was not found in the file of the parent application 08/612,973, which is US Patent 6,150,134. Applicant is requested to provide the priority document.

Claim Rejections - 35 USC § 112

Rejection of claims 17-19 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement **is maintained.**

Applicant's arguments have been fully considered but are not persuasive. The claims were rejected because the current specification does not enable one skilled in the art to use the isolated HCV envelope protein as medicament or a vaccine composition.

Applicant argues that the successful use of HCV envelope proteins or portions thereof as medicaments is known in the art. Applicant directs the Examiner to a number of patents and patent applications that disclose the use of HCV envelope proteins as medicaments. Particularly Applicant directs to Examples 4-6 in the US Patent 6,635,257. Examples 4-6 in the US Patent 6,635,257 disclose immunization/vaccination of HCV infected chimpanzee with E1 (aa 192-326) and E1 from genotype 1b. Examples 15-18 of US Patent 7,101,561 disclose prophylactic utility of E1-vaccination in chimpanzee and generation of immune responses in humans following immunization and boosting with E1 protein. However the claims of the US Patent 6,635,257 or US Patent 7,101,561 do not recite the claimed composition as "vaccine" or the use of the claimed compositions as "medicaments". The recitation of "vaccine" and/ or "medicaments" is used in the specification and/or Examples of US Patent 6,635,257 or US Patent 7,101,561. Furthermore what is disclosed and recited in the claims, specification or examples of US Patent 6,635,257 or US Patent 7,101,561 is irrelevant in the present situation because the currently claimed composition is distinct from the compositions claimed in the US Patent 6,635,257 and US Patent 7,101,561.

The currently claimed composition is an isolated HCV envelope protein or part thereof comprising at least one Cys amino acid, which is reversibly protected by sulfonation. The current specification does not provide working examples showing that the currently claimed composition is in fact effective as vaccine or a medicament. The working examples provided by the

Applicant show purification of HCV E1s after reversible modification of Cys-residues. There is absence of working examples showing that vaccination of animal subjects with isolated HCV envelope proteins E1s or E1p, or parts thereof, comprising at least one Cys amino acid, which is reversibly protected by sulfonation, can result in generation of protective immune responses in the animals. There are no working examples showing that immunization of animals or humans with currently claimed composition, can contribute to clearance or decrease of the viral particles from the infected organs. It is known in the art that even minor modifications or deletions of amino acids within a protein, can drastically alter the immunogenic property of the protein. Additionally treatment of proteins with various organic compounds such those used in sulphonation, may alter immunogenicity of the proteins. Moreover, the residual organic compounds used in sulphonation can be toxic to the animal that is being immunized. Thus without experimental testing, one of ordinary skill in the art cannot reasonably assume that the HCV envelope proteins E1s or E1p, wherein one Cys amino acid is reversibly protected by sulfonation, can in fact induce protective immune responses in an animal. For the above reasons, it appears that undue experimentation would be required to practice the claimed invention with a reasonable expectation of success. Therefore the rejection is maintained.

Claim Rejections - 35 USC § 102

Rejection of claims 12-15 and 23 under 35 U.S.C. 102(b) as being anticipated by Grakoui et al. (Journal of Virology, 1993) **is withdrawn**, because Grakoui et al. art does not teach an isolated HCV envelope protein comprising at least one cysteine amino acid which is reversibly protected by sulfonation.

Rejection of claims 16, 17, 20, 22 under 35 U.S.C. 102(b) as being anticipated by Grakoui et al. (Journal of Virology, 1993) **is maintained.**

Applicant's arguments have been fully considered but fail to persuade. Applicant argues that the cited art does not teach all claim limitations. Claims are drawn to an isolated HCV envelope protein or part thereof comprising at least one Cys amino acid that is reversibly protected and wherein the reversible protection of Cys amino acids is removed. Because the claims require that the reversible protection of Cys amino acids is removed, it is interpreted that the claims are drawn to an isolated HCV envelope protein or part thereof. Garkoui et al. disclose an isolated HCV envelope protein. Thus the claims are anticipated by Grakoui et al.

Regarding claims 17 and 20, it is noted that the intended use of the isolated HCV envelope protein as a medicament and for raising antibodies is not limiting, because it confers no further substance to the claim and thus it is given little patentable weight (see *In re Pearson*, 494 F.2nd 1399, 1403, 181 USPQ 641, 664 (CCPA 1974)).

With regard to claims 22 and 23, which are product by process claims, the product disclosed by the prior art is identical to the claimed product, (even though it is made by a somewhat different process/the prior art is silent on the method of making). There is no evidence to show that the claimed process imparts any patentable distinction between the claimed product and that of the prior art.

M.P.E.P. Section 2113 states that: "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production.

If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985).

For the above reasons the rejection is maintained.

Rejection of claims 12-15 and 23 under 35 U.S.C. 102(e) as being anticipated by Watanabe et al., (US Patent 5,610,009) **is withdrawn**, because Watanabe et al. art does not teach an isolated HCV envelope protein comprising at least one cysteine amino acid which is reversibly protected by sulfonation.

Rejection of claims 16, 17, 20, 22 under 35 U.S.C. 102(e) as being anticipated by Watanabe et al., (US Patent 5,610,009) **is maintained.**

Applicant's arguments have been fully considered but fail to persuade. Applicant argues that the cited art does not teach all claim limitations. Claims are drawn to an isolated HCV envelope protein or part thereof comprising at least one Cys amino acid that is reversibly protected and wherein the reversible protection of Cys amino acids is removed. Because the claims require that the reversible protection of Cys amino acids is removed, it is interpreted that the claims are drawn to an isolated HCV envelope protein or part thereof. Watanabe et al., disclose an isolated HCV envelope protein and particularly E1 protein comprising E1s and E1p (see the entire document, particularly column 3 and 5). Watanabe et al., disclose the use of isolated HCV envelope protein in vaccine composition (see column 4 lines 55-65). Tus the claims are anticipated by Watanabe et al.

Regarding claims 17 and 20, it is noted that the intended use of the isolated HCV envelope protein as a medicament and for raising antibodies is not limiting, because it confers no further substance to the claim and thus it is given little patentable weight (see In re Pearson, 494 F.2nd 1399, 1403, 181 USPQ 641, 664 (CCPA 1974)).

With regard to claims 22 and 23, which are product by process claims, the product disclosed by the prior art is identical to the claimed product, (even though it is made by a somewhat different process/the prior art is silent on the method of making). There is no evidence to show that the claimed process imparts any patentable distinction between the claimed product and that of the prior art.

M.P.E.P. Section 2113 states that: "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production.

If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985).

For the above reasons the rejection is maintained.

New rejection

Claims 12-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed

invention. The claims are drawn to an isolated HCV envelope protein or part thereof comprising at least one Cys amino acid that is reversibly protected by sulphonation. The specification contemplates generation of parts of HCV envelope protein comprising a redox active center [see 0096].

The term "functionally equivalent part thereof" as used herein refers to a part or fragment of said HCV protein that contains in its amino acid sequence at least one cysteine, the redox status of which is variable. In particular, the terms "protein" and "functionally equivalent part thereof" refers to HCV proteins and fragments thereof comprising a redox active center, such as, for example, HCV E1 protein. More particularly, the present invention relates to HCV E1s, and HCV E1p. In this regard, the term "redox active center" as used herein connotates a protein motif with the consensus sequence CXXC.

However, the instant specification provides insufficient description of the specific structures of the claimed parts of an isolated HCV envelope protein. It is apparent that at the time when the current application was filed the Applicant did not have the possession of the claimed parts of HCV envelope protein.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the specification contemplates production of parts of an isolated HCV envelope protein. Based on the knowledge of the HCV proteins, comprising a redox active center that should be comprised within the claimed parts, one of skill in the art would not know what are the complete structures of the claimed parts of the isolated HCV envelope protein. Applicant has not provided the structure-function correlation between the claimed parts and the intended function that the parts of the HCV proteins are

expected to maintain. Accordingly, in the absence of insufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed structure of the encompassed genus of HCV protein parts, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of production of synthesis of the claimed protein parts. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

For the written description requirement, an applicant's specification must reasonably convey to those skilled in the art that the applicant was in possession of the claimed invention as of the date of invention. *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1405 (Fed. Cir. 1997); *Hyatt v. Boone*, 146 F.3d 1348, 1354, 47 USPQ2d 1128, 1132 (Fed. Cir. 1998). In this instance claiming a product based without its known and defined structure or function, does not provide sufficient description of the product. Because Applicants have not provided a representative number of species or the expected function of the claimed genus of parts of HCV proteins, it is apparent that at the time the current invention was made Applicants were not in possession of the claimed products.

Conclusion

Claims 12-15 and 23 are free of prior art of record.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Agnieszka Boesen whose telephone number is 571-272-8035. The examiner can normally be reached on 9:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

AB

Agnieszka Boesen, Ph.D.

1/11/2007

Stacy B. Chen 1/16/07

STACY B. CHEN
PRIMARY EXAMINER